Biocatalytic synthesis of δ-gluconolactone and ε-caprolactone copolymers*

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The biodegradability and biocompatibility properties of ε-caprolactone homopolymers place it as a valuable raw material, particularly for controlled drug delivery and tissue engineering applications. However, the usefulness of such materials is limited by their low hydrophilicity and slow biodegradation rate. In order to improve polycaprolactone properties and functionalities, copolymerization of ε-caprolactone with δ-gluconolactone was investigated. Since enzymatic reactions involving sugars are usually hindered by the low solubility of these compounds in common organic solvents, finding the best reaction medium was a major objective of this research. The optimal copolymerization conditions were set up by using different organic media (solvent and solvents mixtures), as well as solvent free systems that are able to dissolve (completely or partially) sugars, and are nontoxic for enzymes. Native and immobilized lipases by different immobilization techniques from Candida antarctica B and Thermomyces lanuginosus have been used as biocatalyst at 80°C. Although the main copolymer amount was synthesized in DMSO: t-BuOH (20:80) medium, the highest polymerization degrees, up to 16 for the copolymer product, were achieved in solventless conditions. The products, cyclic and linear polyesters, have been characterized by FT-IR and MALDI-TOF MS analysis. The reaction product analysis revealed the formation of cyclic products that could be the major impediment of further increase of the chain length.

Key words: ε-caprolactone, δ-gluconolactone, lipases, biopolymers

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Abbreviations: αw, water activity; ECL, ε-caprolactone; GL, D-glucono-δ-lactone; PCL, poly-(ε-caprolactone); Lipzyme-TL IM, Thermomyces lanuginosus lipase; CALB-Lecta, Candida antarctica lipase B; PPL, porcine pancreatic lipase; TMOS, tetramethoxysilane; OcTMOS, octyl-trimethoxysilane; 3-NH₂PrTMOS, 3-aminopropyltrimethoxysilane; LC, linear copolymer; CC, cyclic copolymer; LH, linear homopolymer; CH, cyclic homopolymer; logP, partition coefficient; Mw, weight average molecular weight; Mn, number average molecular weight; PDI, polydispersity index
Supplementary material

NMR spectra were recorded on a Bruker Avance III spectrometer operating at 500.0 MHz (1H) and 125.0 MHz (13C). The samples were dissolved in DMSO-d6 and the chemical shifts are given in ppm from TMS.

In the $^1$H-NMR spectrum of the reaction product, two doublets at 6.25 ppm and 6.22 ppm, corresponding to the two types of OH groups bounded to the CH (no 14 in the structure depicted in Scheme 1) confirm the formation of the linear/cyclic copolymer (Fig. 4).

Scheme 1. Structure of the linear oligomer formed from one gluconolactone and two caprolactone units
Fig. 4. $^1$H-NMR spectral region (5.6-6.5ppm) of the reaction product (green), ε-caprolactone (red) and δ-gluconolactone (blue)

In the $^1$H-$^1$H-COSY spectra (Fig.5), the coupling of the signals of these protons (6.25 and 6.22 ppm) and of the signals from 5.73 and 5.59 ppm with the signals from 4.66-4.04 ppm (multiplets) corresponding to the protons of CH groups was detected, demonstrating the formation of the reaction product with inserted ring-opened GL unit.
Fig. 5. $^1$H-$^1$H-COSY 2D NMR spectral region (5.1-6.5 ppm/3.8-6.5 ppm) of the reaction product

The shielded or unshielded protons corresponding to the OH groups from the GL unit of the copolymer (in the spectral region 4.03-3.5 ppm, Fig. 6) are present at different chemical shifts compared to the GL raw material, indicating the formation of the cyclic and linear copolymer, respectively.
Fig. 6. $^1$H-NMR (3.0-4.5ppm) spectral region of the reaction product (green), $\varepsilon$-caprolactone (red) and $\delta$-gluconolactone (blue)